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Vesicular Rash in a 28-day-old Girl

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Presentation

A 28-day-old, previously healthy, full-term girl presents to the emergency department after 2 days of irritability and 1 day of a rash. She has had no fevers, hypothermia, cough, congestion, increased work of breathing, easy bleeding or bruising, jaundice, or other symptoms. She was born via a scheduled repeat cesarean delivery at 38 weeks’ gestation after an uncomplicated pregnancy. Her mother received adequate prenatal care and had no serologic evidence of prenatal infections. After 3 days in the well-infant nursery, the child was discharged. No one at home is currently ill; however, the patient’s 8-year-old sister had a “cold sore” ~2 weeks before admission.

On approximately day 10 after birth, the patient’s mother had an outbreak of painful “itchy blisters” that started on her lower back, then spread to the inguinal region and abdomen, appearing most prominently over her cesarean delivery scar. She does not remember whether the rash was unilateral or bilateral. The lesions have scabbed over and resolved. The mother has never had a similar rash in the past and denies a history of herpes or other sexually transmitted infections. Both parents had chickenpox during childhood. The older siblings have been fully immunized. Family history is unremarkable for any immunodeficiencies or inherited childhood diseases.

Physical examination reveals an afebrile, somewhat fussy but consolable girl infant. Vital signs are all within normal range. Skin findings reveal ~20 vesicles with an erythematous base that are scattered over the face (Fig 1), trunk, legs, plantar surfaces (Fig 2), and buttock. The patient has normal work of breathing, no hepatosplenomegaly, and no mucous membrane involvement. The remainder of her physical examination is normal.

Given the patient’s age, vesicular rash, and history of irritability, a full sepsis workup is performed, and the patient is hospitalized. Complete blood cell count with differential, urinalysis, liver function tests, as well as cerebrospinal fluid cell count and differential, glucose level, and protein concentration are unremarkable. A clinical diagnosis is made and later confirmed by laboratory testing.

Figure 1. Scattered vesicles with an erythematous base over the face.

Author Disclosure

Drs King and Thorell have disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.
Diagnosis: Chickenpox (Varicella)

The appearance of the rash (disseminated scattered vesicles on an erythematous base, classically described as “dew drops on a rose petal”) together with the mother’s history of painful itchy blisters consistent with herpes zoster (shingles) and the timing of that exposure were all suggestive of varicella-zoster virus (VZV) infection. Late presentation of transplacentally acquired herpes simplex virus (HSV) skin, eyes, and mouth (SEM) disease as well as postnatally acquired HSV from the sister with a cold sore were considered at the time of admission, although the disseminated nature of the rash made these diagnoses less likely. Conveniently, the recommended treatment for both VZV and HSV infections is acyclovir administered intravenously every 8 hours, with VZV dose being 30 mg/kg per day and HSV dose 60 mg/kg per day. Acyclovir at the higher dosing recommended for HSV was initiated at the time of admission. A positive VZV polymerase chain reaction (PCR) performed on fluid from an unroofed vesicle confirmed the diagnosis.

Differential Diagnosis

The differential diagnosis for an infant presenting with a vesicular rash is broad. In addition to chickenpox, possible diagnoses include HSV infection, enterovirus infection, neonatal scabies, tinea corporis, impetigo, and syphilis, as well as contact dermatitis and rare genetic disorders such as Langerhans cell histiocytosis and incontinentia pigmenti.

The vast majority of neonatal HSV infections are acquired vertically during vaginal delivery, with a minority of infections acquired transplacentally. Almost all vertically infected infants present before age 6 weeks. The three possible manifestations of vertically acquired neonatal HSV are as follows: multiple organ (disseminated), central nervous system (CNS), or SEM disease. Disseminated HSV infection typically develops during the first postnatal week and presents with multiple organ involvement, including liver, lungs, and CNS. Neonatal HSV infection limited to the CNS typically appears during the second or third postnatal week and presents with seizures, lethargy, irritability, tremors, poor feeding, and temperature instability. Neonatal SEM disease usually presents with skin and mucous membrane lesions in the first 2 weeks after birth but may present at any time during the first 6 weeks. Untreated neonatal HSV SEM can progress to CNS or disseminated disease. HSV is both much more common and much more devastating in neonates than VZV.

This patient’s cesarean delivery birth made vertically transmitted HSV less likely. Her presentation at age 4 weeks and (other than irritability) lack of clinical or laboratory features of either disseminated or CNS HSV made these diagnoses unlikely as well. Given her late presentation, cesarean delivery birth, and disseminated nature of the rash, SEM disease also was thought to be unlikely, although possible.

In addition to vertical transmission, infants also can be infected with HSV via horizontal transmission. After direct exposure to HSV-infected lesions or secretions, patients usually have a 2- to 14-day incubation period, after which a vesicular rash appears. Although this scenario fits with the time frame of our patient’s exposure to her sister with a cold sore, HSV was thought to be less likely than VZV given the disseminated nature of the rash.

Varicella

VZV, a member of the herpesvirus family, is highly contagious, spreading via direct contact, airborne droplets, and transplacental passage. While primary VZV infection leads to chickenpox, reactivation of the dormant virus residing in cells of the dorsal root ganglia results in shingles, also called herpes zoster. Shingles classically is a unilateral
rash consisting of grouped vesicles on an erythematous base, covering one to three adjacent dermatomes, often accompanied by pain and pruritus. The patient’s mother had chickenpox in early childhood and likely her painful itchy blisters represented an initial outbreak of shingles. Appearance of shingles during late pregnancy and the early postpartum period is not uncommon and is thought to be secondary to pregnancy-associated maternal immunosuppression.

Once believed to be an inevitable part of childhood, chickenpox has become less common after the introduction of widespread VZV vaccination in 1995. Diagnosis usually is based on clinical presentation, unimmunized status, and exposure history. If necessary, the diagnosis can be rapidly confirmed by vesicular fluid testing by using either VZV PCR or direct fluorescent antibody (DFA) assay. DFA testing is rapid, specific, and sensitive. PCR testing for VZV infection is specific and sensitive but is less available. VZV viral culture is not recommended routinely because it takes several days and is less sensitive than either of the above methods.

**Symptoms**

The prodrome of chickenpox consists of low-grade fevers, headaches, and malaise developing after an incubation period of ~14 to 16 days. One or 2 days later, vesicles appear in crops for 3 to 5 days and tend to cluster in areas of eczema or previous skin trauma. The vesicles eventually become cloudy with cellular debris, involute, and crust over. The rash typically consists of 250 to 500 lesions in different stages of development and resolution. Patients are considered contagious from approximately the day before symptom onset until all lesions crust over.

Although chickenpox generally is a benign self-limited illness, especially in healthy children under age 12 years, hospitalization rates even among these healthy children in the prevaccine era were still approximately two to three per 1,000 cases, with hospitalization rates among adults being two to three times higher. Although disease severity and complications tend to increase with age, they also are more common in children younger than age 1 year and in immunocompromised individuals.

Bacterial superinfection of cutaneous lesions is the most commonly seen complication; varicella pneumonia is the major cause of morbidity and mortality. Although rare, hepatitis, thrombocytopenia, transient cerebellar ataxia, and encephalitis are possible complications. Average deaths from varicella between 1990 and 1996 were 103 per year, with most occurring in immunocompetent children and adults. Both the number of hospitalizations and the number of deaths from varicella has declined by more than 90% in the postvaccination era.

**Perinatal Varicella**

Although maternal chickenpox at any stage of pregnancy could cause intrauterine fetal demise, infection before 20 weeks’ gestation has a ~2% chance of causing congenital varicella syndrome. The classic findings of this syndrome include intrauterine growth restriction, pigmented skin lesions in dermatomal distribution, ocular defects, skeletal abnormalities, and neurologic deficits.

Infants whose mothers develop chickenpox close to the time of delivery are at risk for transplacentally acquired neonatal varicella. Those whose mothers develop chickenpox within 5 days before and 2 days after delivery are at especially high risk for overwhelming varicella infection, with a mortality rate as high as 30%. These infants are likely exposed to a significant transplacental viral load without the benefit of passive maternal varicella antibody. Infants whose mothers contract varicella outside of that time period are more likely to have acquired maternal antibodies and to have less severe disease.

Chickenpox presenting after the second week after birth is more likely from postnatal direct or droplet exposure than from transplacental acquisition. Our patient likely acquired varicella by direct contact with her mother’s zoster lesions. Since she likely acquired maternal antibodies as well, her disease course was mild. Because of their relative immunologic immaturity, however, all neonates are considered to be at increased risk for severe varicella as well as for early development of shingles.

**Treatment**

Exposed individuals without a previous history of either chickenpox or VZV vaccination should be immunized, unless immunization is contraindicated. Immunoprophylaxis with VZV immunoglobulin should be administered to people at risk for severe disease after exposure to chickenpox or herpes zoster and should be given within 96 hours of exposure. People at risk include immunocompromised individuals, those receiving chronic systemic corticosteroids, varicella antibody negative pregnant women, premature infants born to varicella antibody negative women, and infants whose mothers develop chickenpox (not herpes zoster) within 5 days before and 2 days after delivery. VZV immunoglobulin is not indicated for healthy
infants exposed postnatally. If VZV immunoglobulin is not available, intravenous immunoglobulin may be given for high-risk exposures.

The decision to administer antiviral therapy depends on the patient’s risk factors for severe disease as well as the timing of initial presentation. Because viral replication ceases within 3 days after the rash onset in immunocompetent hosts, antiviral drugs have a narrow therapeutic window to be effective. If indicated, treatment should be instituted as soon as possible. A 5-day course of oral acyclovir should be considered in otherwise healthy individuals at increased risk for moderate-to-severe chickenpox: children >12 years of age and adults; individuals with chronic skin or pulmonary disorders; those receiving chronic salicylate therapy; and those on short, intermittent, or aerosolized corticosteroid therapy. A 7- to 10-day course of intravenous acyclovir (30 mg/kg per day in three divided doses IV) should be considered for those at risk for severe or disseminated disease.

Intravenous acyclovir is indicated for varicella infection in infants born to mothers who experience chickenpox from 5 days before until 2 days after delivery. There is little information on the use of acyclovir in other infants with chickenpox. Because infants may experience more severe or complicated disease, some experts recommend acyclovir use for this population as well.

Patient Course

The patient was admitted to the hospital for acyclovir therapy as well as antibiotic therapy for possible bacterial sepsis. Airborne and contact isolation was instituted based on clinical suspicion of chickenpox. This suspicion was further supported when the infant developed new crops of vesicles during the first day of hospitalization while older vesicles became cloudy. All lesions crusted over by the end of the third hospital day. Antibiotics were discontinued after bacterial cultures of blood, urine, and cerebrospinal fluid revealed no growth. HSV PCR from vesicle, serum, and cerebrospinal fluid was negative. The patient did not develop bacterial superinfection of the lesions. Due to her young age, she received a 10-day course of acyclovir, which was changed to oral therapy at discharge after all lesions were crusted. She recovered without any complications or scars. Because of her early onset of chickenpox, the patient is at increased risk of early manifestation of shingles.

Summary

- Possible causes of a vesicular rash in an infant include the following: herpes simplex virus (HSV), varicella-zoster virus (VSV), enterovirus, neonatal scabies, tinea corporis, syphilis, contact dermatitis, and impetigo, as well as rare genetic disorders such as Langerhans cell histiocytosis and incontinentia pigmenti. History, particularly of exposures, and physical examination can point to the most likely diagnosis.
- The typical course of chickenpox includes direct or droplet exposure; a 14- to 16-day latent period; a 1- to 2-day prodrome of low-grade fevers, headaches, and malaise; and the subsequent appearance of a vesicular rash, classically described as dew drops on a rose petal.
- Chickenpox can be confirmed rapidly by vesicular fluid testing using either VZV polymerase chain reaction or direct fluorescent antibody. Viral culture is less sensitive than either of these methods.
- The decision whether to use antiviral treatment is based on the patient’s risk factors for severe disease as well as the timing of presentation. If indicated, treatment should be initiated as soon as possible. Treatment options include acyclovir for those at risk for moderate-to-severe disease as well as VZV immunoglobulin for those at risk for severe disease.
- Patients are contagious from approximately the day before symptom onset until the time all the lesions are crusted over. Airborne and contact precautions are necessary for hospitalized patients. A history of exposure to individuals at risk for severe disease should be sought in any patient suspected of having chickenpox.

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